

Docket No.: A7542.0000/P001-E (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Ginette Serrero

Application No.: Not Yet Assigned

Group Art Unit: 1642

Filed: April 4, 2001

Examiner: M. Wells

For: 88KDA TUMORIGENIC GROWTH

FACTOR AND ANTAGONISTS

REQUEST TO USE COMPUTER READABLE FORM FROM ANOTHER APPLICATION

ATTN: Application Processing Division Assistant Commissioner for Patents

Washington, DC 20231

Dear Sir:

The computer readable form in this divisional application, filed April 4, 2001, is identical with that filed in application numbers 08/991,862 filed on December 16, 1997 which is a continuation-in-part application of U.S. application serial number 08/863,079 filed on May 23, 1997. In accordance with 37 CFR 1.821(e), please use the only computer readable form filed in the applications as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the computer readable form that will be used for the instant application. A paper copy of the Sequence Listing is included in a separately filed preliminary amendment for incorporation into the specification.

Dated: April 4, 2001

Respectfully submitted,

James W. Brady, Jr

Registration No.: 32,115

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Attorneys for Applicant



Atty. Docket No: Z9996.488/PQ01-A

In re patent application of
Serrero, Ginette

Serial No. 08/991,862

Filed: December 16, 1997

For: 88 KDA TUMORIGENIC GROWTH FACTOR AND ANTAGONISTS

STATEMENT TO SUPPORT FILING AND SUBMISSION IN ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents Washington, D.C. 20231
Box SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

- the submission, filed herewith in accordance with 37
 C.F.R. § 1.821(g), does not include new matter;
- 2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same; and
- 3. all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

. 08/991,

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

.

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Intellectual Property Services
1500A Lafayette Road
Suite 262
Portsmouth, N.H.
800-318-3021

2



SEQUENCE LISTING



<110>	Serrero,	Ginette
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<120> 88 KDA TUMORIGENIC GROWTH FACTOR AND ANTAGONISTS

<130> Z9996.488/P001-A

<140> 08/991,862

<141> 1997-12-16

<150> 08/863,862

<151> 1997-05-23

<160> 17

<170> PatentIn Ver. 2.0

<210> 1

<211> 2137

<212>.DNA

<213> Mouse epithelin/granulin

<220>

<221> CDS

<222> (23)..(1789)

<223> The sequence is identical to that of the published mouse granulin except for one nucleotide (T instead of G) at position 1071 of GP88 cDNA (position 1056 of mouse granulin).

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Met Trp Val Leu Met Ser Trp Leu Ala Phe

1 5 10

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Ala Ala Gly Leu Val Ala Gly Thr Gln Cys Pro Asp Gly Gln Phe Cys
20 25

cct gtt gcc tgc tgc ctt gac cag gga gga gcc aac tac agc tgc tgt 148 Pro Val Ala Cys Cys Leu Asp Gln Gly Gly Ala Asn Tyr Ser Cys Cys 30 30 35

aac cct ctt ctg gac aca tgg cct aga ata acg agc cat cat cta gat 196
Asn Pro Leu Leu Asp Thr Trp Pro Arg Ile Thr Ser His His Leu Asp
45 50 55

ggc tcc tgc cag acc cat ggc cac tgt cct gct ggc tat tct tgt ctt 244
Gly Ser Cys Gln Thr His Gly His Cys Pro Ala Gly Tyr Ser Cys Leu
60 65 70

ctc act gtg tct ggg act tcc agc tgc tgc ccg ttc tct aag ggt gtg

Leu Thr Val Ser Gly Thr Ser Ser Cys Cys Pro Phe Ser Lys Gly Val

80 85 90

tct tgt ggt gat ggc tac cac tgc tgc ccc cag ggc ttc cac tgt agt
Ser Cys Gly Asp Gly Tyr His Cys Cys Pro Gln Gly Phe His Cys Ser
100 105

1

"				. •	'		
gca gat go Ala Asp G	g aaa to y Lys So 110	er Cys Phe	cag at Gln Me	et Ser As	t aac ccc p Asn Pro	tty ggt Leu Gly 120	gct 388 Ala
Val Gln C	gt cct g vs Pro G 25	gg agc cac ly Ser Glr	g ttt ga n Phe Gl 130	aa tgt cc lu Cys Pr	t gac tct o Asp Ser 135	gcc acc Ala Thr	tgc 436 Cys
tgc att a Cys Ile M 140	g gtt g et Val A	at ggt too sp Gly Se: 14	r Trp G	ga tgt tg ly Cys Cy	t ccc atg s Pro Met 150	ccc cag Pro Gln	gcc 484 Ala
tct tgc t Ser Cys C 155	gt gaa g ys Glu A	gac aga gt Asp Arg Va 160	g cat to	gc tgt co ys Cys Pr 10	cc cat ggg co His Gly	gcc tcc Ala Ser	tgt 532 Cys 170
gac ctg g Asp Leu V	al His T	aca cga tg Thr Arg Cy 175	c gtt to s Val S	ca ccc ac er Pro Th 180	eg gge acc nr Gly Thr	cac acc His Thr 185	cta 580 Leu
cta aag _s a Leu Lys I	ag ttc o ys Phe I 190	cct gca ca Pro Ala Gl	n Lys T	cc aac ac hr Asn Se 95	gc gca gtg er Ala Val	tct ttg Ser Leu 200	cct 628
Phe Ser V	tc gtg (al Val (05	tgc cct ga Cys Pro As	t gct ap Ala L 210	ag acc corys Thr G	ag tgt ccc ln Cys Pro 215	Asp Asp	tct 676 Ser
acc tgc f Thr Cys (220	gt gag Cys Glu	cta ccc ac Leu Pro Th 22	ır Gly I	aag tat g Lys Tyr G	gc tgc tgt ly Cys Cys 230	cca atg Pro Met	ccc 724 Pro
aat gcc Asn Ala 235	itc tgc [le Cys	tgt tcc ga Cys Ser As 240	ac cac o sp His I	Leu His C	gc tgc ccc Cys Cys Pro 145	cag gad Gln Asp	2 act 772 Thr 250
gta tgt Val Cys	gac ctg Asp Leu	atc cag a Ile Gln S 255	gt aag (er Lys (tgc cta t Cys Leu S 260	cc aag aad Ser Lys Asi	tac acc n Tyr Thi 26	r Inr
gat ctc Asp Leu	ctg acc Leu Thr 270	aag ctg c Lys Leu P	ro Gly	tac cca q Tyr Pro \ 275	gtg aag gad Val Lys Gla	g gtg aad u Val Ly 280	g tgc 868 s Cys
gac atg Asp Met	gag gtg Glu Val 285	agc tgc c Ser Cys F	ct gaa ro Glu 290	gga tat a Gly Tyr '	acc tgc tg Thr Cys Cy 29	s Arg Le	c aac 916 u Asn
act ggg Thr Gly 300	gcc tgg Ala Trp	Gly Cys C	gt cca Cys Pro	ttt gcc Phe Ala	aag gcc gt Lys Ala Va 310	gʻtgt tg l Cys Cy	t gac 964 s Asp
gat cac Asp His 315	att cat Ile His	tgc tgc c Cys Cys I 320	ccg gca Pro Ala	Gly Phe	cag tgt ca Gln Cys Hi 325	c aca ga s Thr Gl	g aaa 1012 u Lys 330
gga acc Gly Thr	tgc gaa Cys Glu	atg ggt a Met Gly 335	atc ctc Ile Leu	caa gta Gln Val 340	ggg tgg at Gly Trp Me	et Lys Ly	ng gtc 1060 ys Val 15

											•					
ata d	gcc Ala	ccc Pro	ctc Leu 350	cg Arg	etg (cca (Pro i	Asp	cca (Pro (355	cag Gln	atc Ile	ttg Leu	aag Lys	Ser 360	gat Asp	aca Thr	
cct Pro	tgt Cys	gat Asp 365	gac Asp	ttc Phe	act . Thr	Arg	tgt Cys 370	cct . Pro '	aca Thr	aac Asn	aat Asn	acc Thr 375	tgc Cys	tgc Cys	aaa Lys	1156
ctc Leu	aat Asn 380	tct Ser	G] À dàd	gac Asp	tgg Trp	ggc Gly 385	tgc Cys	tgt Cys	ccc Pro	atc Ile	cca Pro 390	gag Glu	gct Ala	gtc Val	tgc Cys	1204
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cag Gln	ggg Gly	tac Tyr	tgt Cys	cag Gln 415	aag Lys	gga Gly	gac Asp	aca Thr	atg Met 420	gtg Val	gct Ala	ggc Gly	ctg Leu	gag Glu 425	гуs	1300
ata Ile	cct Pro	gcc	cgc Arg 430	cag Gln	aca Thr	acc Thr	ccg Pro	ctc Leu 435	caa Gln	att Ile	gga Gly	gat Asp	atc Ile 440	Gly	tgt Cys	1348
gac Asp	cag Gln	cat His	Thr	agc Ser	tgc Cys	cca Pro	gta Val 450	ggg	caa Gln	acc Thr	tgc Cys	tgc Cys 455	Pro	ago Ser	ctc Leu	1396
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gac Asp 475	Arg	caç Glr	g cac n His	tgt Cys	tgc Cys 480	Pro	gcc Ala	ggg	tac	acc Thi	c Cys	c aad s Asi	gto n Val	g aad L Ly:	g gcg s Ala 490	1492
agg Arg	acc Thr	tgt Cy:	t gaq s Glu	g aag 1 Lys 495	Asp	gto Val	gat Asp	ttt Phe	atc 11e 500	e Gl	g cct n Pro	t cc	c gte o Va	g ct l Le 50	c ctg u Leu 5	1540
acc Thr	cto Le	c gg u Gl	c cct y Pro	o Lys	g gtt s Val	ggç Gly	g aat y Asr	gtg n Val	. Gl	g tg ı Cy	t gg s Gl	a ga y Gl	a gg u G1 52	у Ні	t ttc s Phe	1588
tgc Cys	c car s Hi:	t ga s As 52	p As	c cad	g aco	c tgi	t tgi s Cy: 53	s Lys	a gad s Asj	c ag p Se	t gc r Al	a gg a Gl 53	y Va	c tg l Tr	g gcc p Ala	1636
tgo Cys	c tg s Cy 54	s Pr	c ta o Ty	c ct r Le	a aad u Ly:	g gg s G1 54	y Va	c tgo l Cy:	c tg s Cy	t ag s Ar	a ga g As 55	p Gl	ja ⊹cç .y Ar	rt ca ng Hi	ic tgt is Cys	1684
tge Cy: 55!	s Pr	c gg o Gl	ıt gg y Gl	c tt y Ph	с са е Ні 56	s Cy	t tc s Se	a gcer Al	c ag a Ar	g gg g G1 56	y Th	ec aa nr Ly	ag to	gt ti ys Le	cg cga eu Arg 570	1732
aa Ly	g aa s Ly	ig at 's Il	t co le Pr	t cg o Ar 57	g Tr	g ga p As	c at p Me	g tt t Ph	t tt e Le 58	u Aı	gg ga rg As	at co sp Pi	cg gi ro Va	al P	ca aga ro Arg 85	1780

ccg cta ctg taaggaagg ctacagactt aaggaactcc acagtcctg.

gaaccetgtt cegagggtac ceactactea ggeeteetta gegeeteete eeetaacgte 1889

teeceeggeet acteateetg agteaceeta teaceatggg aggtggagee teaaactaaa 1949

acettettt atggaaagaa ggetetggee aaaageeeeg tateaaactg ceatteette 2009

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aaaaaaaaa

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Asp Gln Gly Gly Ala Asn Tyr Ser Cys Cys Asn Pro Leu Leu Asp Thr
35 40 45

Trp Pro Arg Ile Thr Ser His His Leu Asp Gly Ser Cys Gln Thr His 50 55 60

Gly His Cys Pro Ala Gly Tyr Ser Cys Leu Leu Thr Val Ser Gly Thr 65 70 75 80

Ser Ser Cys Cys Pro Phe Ser Lys Gly Val Ser Cys Gly Asp Gly Tyr 85 90 95

His Cys Cys Pro Gln Gly Phe His Cys Ser Ala Asp Gly Lys Ser Cys
100 105 110

Phe Gln Met Ser Asp Asn Pro Leu Gly Ala Val Gln Cys Pro Gly Ser 115 120 125

Gln Phe Glu Cys Pro Asp Ser Ala Thr Cys Cys Ile Met Val Asp Gly 130 135 140

Ser Trp Gly Cys Cys Pro Met Pro Gln Ala Ser Cys Cys Glu Asp Arg 145 150 155 160

Val His Cys Cys Pro His Gly Ala Ser Cys Asp Leu Val His Thr Arg

Cys Val Ser Pro Thr Gly Thr His Thr Leu Leu Lys Lys Phe Pro Ala 180 185 190

Gln Lys Thr Asn Ser Ala Val Ser Leu Pro Phe Ser Val Val Cys Pro 195 200 205 Asp Ala Lys Thr Glacys Pro Asp Asp Ser Thr Cys Cys Gla Leu Pro 210 215 220

Thr Gly Lys Tyr Gly Cys Cys Pro Met Pro Asn Ala Ile Cys Cys Ser 225 230 235 240

Asp His Leu His Cys Cys Pro Gln Asp Thr Val Cys Asp Leu Ile Gln 245 250 255

Ser Lys Cys Leu Ser Lys Asn Tyr Thr Thr Asp Leu Leu Thr Lys Leu 260 265 270

Pro Gly Tyr Pro Val Lys Glu Val Lys Cys Asp Met Glu Val Ser Cys 275 280 285

Pro Glu Gly Tyr Thr Cys Cys Arg Leu Asn Thr Gly Ala Trp Gly Cys 290 295 300

Cys Pro Phe Ala Lys Ala Val Cys Cys Asp Asp His Ile His Cys Cys 305 310 315

Pro Ala Gly Phe Gln Cys His Thr Glu Lys Gly Thr Cys Glu Met Gly 325 330 335

Ile Leu Gln Val Gly Trp Met Lys Lys Val Ile Ala Pro Leu Arg Leu 340 345 350

Pro Asp Pro Gln Ile Leu Lys Ser Asp Thr Pro Cys Asp Asp Phe Thr 355 360 365

Arg Cys Pro Thr Asn Asn Thr Cys Cys Lys Leu Asn Ser Gly Asp Trp 370 375.

Gly Cys Cys Pro Ile Pro Glu Ala Val Cys Cys Ser Asp Asn Gln His 385 390 395 400

Cys Cys Pro Gln Gly Phe Thr Cys Leu Ala Gln Gly Tyr Cys Gln Lys 405 410 415

Gly Asp Thr Met Val Ala Gly Leu Glu Lys Ile Pro Ala Arg Gln Thr 420 425 430

Thr Pro Leu Gln Ile Gly Asp Ile Gly Cys Asp Gln His Thr Ser Cys 435 440 445

Pro Val Gly Gln Thr Cys Cys Pro Ser Leu Lys Gly Ser Trp Ala Cys 450 455 460

Cys Gln Leu Pro His Ala Val Cys Cys Glu Asp Arg Gln His Cys Cys 465 470 475 480

Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala Arg Thr Cys Glu Lys Asp 485 490 495

Val Asp Phe Ile Gln Pro Pro Val Leu Leu Thr Leu Gly Pro Lys Val 500 505 510

Gly Asn Val Glu Cys Gly Glu Gly His Phe Cys His Asp Asn Gln Thr 515 520 525

```
Cys Cys Lys Asp Ser Ala Gly Val Trp Ala Cys Cys Pro Tyr Leu Lys
                       . 535
Gly Val Cys Cys Arg Asp Gly Arg His Cys Cys Pro Gly Gly Phe His
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Cys Ser Ala Arg Gly Thr Lys Cys Leu Arg Lys Lys Ile Pro Arg Trp
                                     570
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                                 585
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<213> mouse granulin
<220>
<221> PEPTIDE
<222> (1)...(19)
 <223> Internal peptide of mouse GP88 used to raise the
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       immunoaffinity step.
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 Lys Lys Val Ile Ala Pro Arg Arg Leu Pro Asp Pro Gln Ile Leu Lys
   1
 Ser Asp Thr
 <210> 4
 <211> 12
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 <221> PEPTIDE
 <222> (1)..(12)
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                    5
  <210> 5
  <211> 14
  <212> PRT
  <213> mouse granulin
  <220>
  <221> PEPTIDE
  <222> (1)..(14)
  <223> Internal peptide of mouse GP88 used to raise the
        antisera against the GP88 used in the
```

والمراز المعهد المعادات

immunoaffinity step.

<210> 9 <211> 27 <212> DNA

<213> mammalian

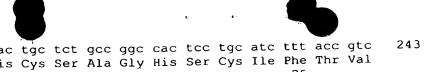
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<220>
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      neutralizing anti-human GP88 monoclonal antibody.
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                   5
                                      10
Arg Asp Val
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       neutralizing anti-human GP88 monoclonal antibody.
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  <212> DNA
 <213> mammalian
  <220>
  <221> primer
  <222> (1)..(24)
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24

7

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<220> <221> primer <222> (1)(27) <223> Antisense primer oligonucleotide primer	
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<210> 12 <211> 25 <212> DNA <213> mammalian	
<220> <221> primer <222> (1)(25) <223> primer	
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tgc tgc ctg gac ccc gga gga gcc agc tac agc tgc tgc cgt ccc ctt Cys Cys Leu Asp Pro Gly Gly Ala Ser Tyr Ser Cys Cys Arg Pro Leu 30 35 40	147
ctg gac aaa tgg ccc aca aca ctg agc agg cat ctg ggt ggc ccc tgc Leu Asp Lys Trp Pro Thr Thr Leu Ser Arg His Leu Gly Gly Pro Cys 50 55 60	195



cag (Gln	gtt Val	gat Asp	gcc Ala 65	His	tġ Cy	c t	ct Ser	gcc Ala	ggc Gly 70	H	ac is	tcc Ser	tgc Cys	ato Ile	e P	tt he 75	acc Thr	gt Vä	c al	243
tca Ser	ggg Gly	act Thr 80	Ser	agt Ser	t tg	jc t /s (tgc Cys	ccc Pro 85	ttc Phe	C P	ca ro	gag Glu	gcc Ala	gte Va 9	I A	ca la	tgc Cys	g(gg Ly	291
gat Asp	ggc Gly 95	cat	cac His	tgo Cys	e to	/S	cca Pro 100	cgg Arg	ggc	t P	tc	cac His	tgc Cys 105	Se	t g r A	ca la	gac Asp	g G	gg 1 y	339
cga Arg 110	tcc Ser	t g c	tto Phe	caa e Gli	n A	ga rg 15	tca Ser	ggt Gly	aac Asr	: a	ac Asn	tcc Ser 120	gtg Val	gg Gl	t g y <i>F</i>	gcc Ala	ato	G	ag ln 25	387
tgc Cys	cct Pro	gat Asp	agt Se:	c ca c Gl 13	n P	tc he	gaa Glu	tgc Cys	cc Pro) <i>F</i>	gac Asp 135	ttc Phe	tcc Ser	ac Th	g t	gc Cys	tgt Cys 140	. v	tt al	435
atg Met	gtc Val	ga As	t gg p Gl 14	y Se	c t r T	gg rp	ggg Gly	tgc Cys	tge Cy: 15	s I	ccc Pro	atg Met	Pro	c ca	Ln A	gct Ala 155	tco Ser	c t	gc ys	483
tgt Cys	gaa Glu	ga As	c ag p Ar 0	g gt g Va	g c	ac	tgc Cys	tgt Cys 165	Pr	g (cac His	ggt Gly	gco Ala	a Pi	ne 70	tgc Cys	ga . As	c c p I	etg Leu	531
gtt Val	cac His	Th	c cg r Ar	c to	jc a /s I	itc []e	aca Thr 180	Pro	c ac	g r	ggc Gly	aco Thi	c ca Hi 18	s P	cc ro	ctg Leu	gc Al	a a	aag Lys	579
aag Lys 190	Le	c cc ı Pr	t go	c ca .a Gi	ln <i>I</i>	agg Arg 195	act Thr	aad Asi	c ag n Ar	g	gca Ala	gto Va: 20	T AT	c t a L	tg eu	tcc Ser	ag Se	I	tcg Ser 205	627
gto Val	ate L Me	g to t Cy	gt co ys Pi	10 A	ac o sp i	gca Ala	cgg	g to g Se	c cọ r Ai	g	tgo Cys 215	s Pr	t ga o As	t g p G	gt	tct Sei	ac Th 22	ır	tgc Cys	675
tgt Cys	c ga s Gl	g ct u Le	tg ce eu Pi 2	cc a ro S 25	gt er	ggg Gly	aaq Ly:	g ta s Ty	r G	дс 1 у 30	tgo Cy:	c tg s Cy	c co	a a o M	tg let	Pro 23	o As	ac sn	gcc Ala	723
acc Th:	c tg r Cy	s C	gc t ys S 40	cc g er A	at	cac His	c cto	g ca u Hi 24	s C	gc ys	tg Cy	c cc s Pr	c ca o Gi	Ln A	gac Asp 250	ac Th	t gi	tg al	tgt Cys	771
ga As	c ct p Le 25	u I	tc c le G	ag a ln S	igt Ser	aaq Ly:	g tg s Cy 26	s Le	c t eu S	cc er	aa Ly	g ga s Gl	Lu A	ac o sn <i>i</i> 65	gct Ala	ac Th	са r Т	cg hr	gac Asp	819
ct Le 27	u Le	c a eu T	ct a hr I	ag o ys I	ctg Leu	cc Pro 27	o Al	g ca .a H:	ac a is T	ca hr	gt Va	1 G	gc g Ly A 80	at sp	gtg Val	aa Ly	a t 's C	gt ys	gac Asp 285	867
at Me	g ga t G	ag ç lu V	itg a /al.s	Ser (tgc Cys 290	cc Pr	aga oAs	at go sp G	gc t ly T	at `yr	ac Th	r C	gc t ys C	gc	cgt Arç	ct J Le	eu C	ag 1n 800	tcg Ser	, 915

				'3									U			
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cac His	ata Ile	cac His 320	tgc Cys	tgt Cys	ccc Pro	gcg Ala	ggg Gly 325	ttt Phe	acg Thr	tgt Cys	gac Asp	acg Thr 330	cag Gln	aag Lys	ggt Gly	1011
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Gly	cag Gln 415	Cys	cag Gln	cga Arg	gga Gly	agc Ser 420	Glu	atc Ile	gtg Val	gct Aļa	gga Gly 425	, Let	g gag n Glu	aaçı Lys	atg Met	1299
cct Pro 430	Ala	cgo Aro	c cgc g Arg	ggt Gly	tcc Ser 435	Leu	tcc Ser	cac His	CCC	aga Arç	, Asp	ato	e Gly	tgt / Cys	gac Asp 445	1347
caç Glr	cac His	c acc	c ago	tgc Cys 450	Pro	gto Val	g ggc	gga Gly	acc Thr 455	Cys	c tgo	c cco	g ago o Sei	c cag c Gli 460	g ggt n Gly D	1395
ggg Gly	g ago / Se:	tge Tr	g gco p Ala 46	a Cys	tgo Cys	caç Glr	g tto n Lei	g ccc u Pro 470	His	get s Ala	t gte a Va	g tg 1 Cy	c tg s Cy: 47	s GI	g gat u Asp	1443
cgo Aro	c ca g Gl:	g ca n Hi 48	s Cy	c tgo s Cys	c ccc	g gct	t ggo a Gly 48	у Ту	c acc	c tg r Cy	c aa s As	c gt n Va 49	l Ly	g gc s Al	t cga a Arg	1491
tc Se	c tg r Cy 49	s Gl	g aa u Ly	g gaa s Gli	a gto u Va	g gt l Va 50	l Se	t gco	c ca a Gl	g cc n Pr	t gc o Al 50	a Th	c tt	c ct e Le	g gcc u Ala	1539
cg Ar 51	g Se	c cc r Pr	t ca o Hi	c gt s Va	g gg 1 Gl 51	y Va	g aa l Ly	g ga s As	c gt p Va	g ga 1 G1 52	u Cy	ıt gç 's Gl	gg ga .y Gl	a gg u Gl	ga•cac y His 525	1587
tt Ph	c tg e Cy	c ca 's Hi	it ga .s As	t aa sp As 53	n Gl	g ac n Th	c tg ir Cy	ıc tg rs Cy	c cg s Ar 53	g As	ic aa sp As	ac co sn Ai	ga ca cg Gl	ın Gl	gc tgg Ly Trp 10	1635

gcc tgc tg Ala Cys Cy	gt ccc ys Pro 545	tac ga Tyr Al	c cag la Gln	Gly V	tc to al Cy 50	, gt tg ys Cy	t gct s Ala	t gat a Asp	cgg Arg A	agc c	ac is	1683
tgc tgt co Cys Cys P: 5	ct gct ro Ala 60	ggc tt Gly Ph	tc cgc ne Arg	tgc g Cys <i>F</i> 565	gca co Ala A	gc ag rg Ar	g Gl	t acc y Thr 570	aag t Lys (gt t Cys L	tg eu	1731
cgc agg g Arg Arg G 575	ag gcc lu Ala	ccg co Pro A	gc tgg rg Trp 580	Asp A	gee e Ala P	ct tt ro Le	g ag eu Ar 58	g Asp	cca (Pro	gcc t Ala I	tg .eu	1779
aga cag c Arg Gln L 590		tgagg	gacag	tactg	aagac	toto	gcagc	cc to	gggac	ccc		1831
actcggagg	g tgcc	ctctgc	tcago	geetee	ctag	cacct	ic co	ectaa	cca a	attct	tecet	1891
ggaccccat	t ctga	gctccc	catca	accatg	ggag	gtgg	gg co	ctcaat	cta a	ggcc	cttcc	1951
ctgtcagaa	ıd aada	ttgagg	caaaa	agccca	ttac	aagct	tg co	catccc	ctc c	ccgt	ttcag	2011
tggaccctg	gt ggcc	aggtgc	tttt	ccctat	ccad	caggg	gt gt	ttgtg	tgt t	gggt	gtgct	2071
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Pro Met Pro Gln Ala Ser Cys Cystalu Asp Gly Ser Trp Gly Cys Arg Val His Cys Cys Pro His Gly Ala Phe Cys Asp Leu Val His Thr Arg Cys Ile Thr Pro Thr Gly Thr His Pro Leu Ala Lys Lys Leu Pro 185 Ala Gln Arg Thr Asn Arg Ala Val Ala Leu Ser Ser Ser Val Met Cys Pro Asp Ala Arg Ser Arg Cys Pro Asp Gly Ser Thr Cys Cys Glu Leu Pro Ser Gly Lys Tyr Gly Cys Cys Pro Met Pro Asn Ala Thr Cys Cys Ser Asp His Leu His Cys Cys Pro Gln Asp Thr Val Cys Asp Leu Ile 250 Gln Ser Lys Cys Leu Ser Lys Glu Asn Ala Thr Thr Asp Leu Leu Thr Lys Leu Pro Ala His Thr Val Gly Asp Val Lys Cys Asp Met Glu Val Ser Cys Pro Asp Gly Tyr Thr Cys Cys Arg Leu Gln Ser Gly Ala Trp 295 Gly Cys Cys Pro Phe Thr Gln Ala Val Cys Cys Glu Asp His Ile His 310 Cys Cys Pro Ala Gly Phe Thr Cys Asp Thr Gln Lys Gly Thr Cys Glu 330 Gln Gly Pro His Gln Val Pro Trp Met Glu Lys Ala Pro Ala His Leu 345 Ser Leu Pro Asp Pro Gln Ala Leu Lys Arg Asp Val Pro Cys Asp Asn 360 Val Ser Ser Cys Pro Ser Ser Asp Thr Cys Cys Gln Leu Thr Ser Gly 375 370 Glu Trp Gly Cys Cys Pro Ile Pro Glu Ala Val Cys Cys Ser Asp His 395 Gln His Cys Cys Pro Gln Arg Tyr Thr Cys Val Ala Glu Gly Gln Cys Gln Arg Gly Ser Glu Ile Val Ala Gly Leu Glu Lys Met Pro Ala Arg Arg Gly Ser Leu Ser His Pro Arg Asp Ile Gly Cys Asp Gln His Thr

440

455

Ser Cys Pro Val Gly Gly Thr Cys Cys Pro Ser Gln Gly Gly Ser Trp

Ala Cys Cys Gln Leu Chis Ala Val Cys Cys Glu Asp 465

Cys Cys Pro Ala Gly Tyr Thr Cys Asn Val Lys Ala Arg Ser Cys Glu 495

Lys Glu Val Val Ser Ala Gln Pro Ala Thr Phe Leu Ala Arg Ser Pro 500 505 510

His Val Gly Val Lys Asp Val Glu Cys Gly Glu Gly His Phe Cys His 515 520 525

Asp Asn Gln Thr Cys Cys Arg Asp Asn Arg Gln Gly Trp Ala Cys Cys 530 535 540

Pro Tyr Ala Gln Gly Val Cys Cys Ala Asp Arg Arg His Cys Cys Pro 545 550 555 560

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Ala Pro Arg Trp Asp Ala Pro Leu Arg Asp Pro Ala Leu Arg Gln Leu 580 585 590

Leu